

# Hyperbilirubinemic Stain: Location and Extent in Dental Tissues

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**Objective:** The purpose of the present manuscript is to describe the location and extent of hyperbilirubinemic stain in a primary molar of a 3-year-old who was diagnosed with cystic fibrosis shortly after birth, subsequently developed liver disease and hyperbilirubinemia, and received a liver transplant at age 10-months.

**Study design:** Clinical and histological assessments were performed to evaluate the location and extent of hyperbilirubinemic stain in an extracted primary molar. **Results:** The clinical image, and macroscopic and microscopic histological examinations of a primary molar showed hyperbilirubinemic staining of enamel and of the coronal dentin that developed between birth and when the liver transplant took place, irregular dentin tubules, and an irregular cementum-dentinal junction. **Conclusions:** The findings of the present manuscript indicate that hyperbilirubinemic staining of primary teeth affects dental hard tissues at the time of their calcification, and the clinical picture of the stain may be related to stained enamel and/or dentin, and underlying stained dentin visible through translucent unstained enamel.

**Keywords:** Cystic fibrosis, liver, hyperbilirubinemia, staining.

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## INTRODUCTION

Cystic fibrosis (CF) is an inherited disease of secretory glands caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) and is the most common serious autosomal recessive disorder in the Caucasian population (1 in every 3000 live births). The tissues affected by CF include sweat glands, intestine, pancreatic ducts, respiratory epithelia, submandibular glands, uterus, and bile duct.<sup>1-5</sup> Lung disease represents the main cause of morbidity and mortality in CF. While CF-associated liver disease typically has little clinical significance, it may in some cases lead to hepatic failure and contributes to CF-related mortality in 2.5% of cases.<sup>1,2,5,6</sup>

Liver disease may lead to hyperbilirubinemia (HypB) as

the result of the accumulation of breakdown products of hemolysis, and sustained HypB is known to have protean consequences in the pediatric patient including discoloration of the hard and soft tissues.<sup>7-9</sup> The effects of HypB on soft tissues of the oral cavity may resolve with correction of the underlying metabolic defect, however, mineralized structures are permanently affected.<sup>9</sup> The literature appears to be inconsistent with regards to the precise location of the intrinsically stained mineralized tissue, with some reports identifying localization in the enamel, dentin, or both.<sup>9-11</sup> Herein, we describe the clinical image and histopathology of a tooth from a 3-year-old boy with HypB related green discoloration of the primary dentition, as a consequence of CF related hepatic failure.

## Case description

The parents of a 3-year-old boy accompanied their child to the dental clinic due to pain and swelling on the lower right quadrant. Pertinent health history included developmental delay, and diagnosis of cystic fibrosis shortly after birth. In a short period of time, hepatic function deterioration ensued accompanied by sustained HypB, and the child underwent orthopic liver transplantation by age 10 months.

Upon oral examination, multiple carious lesions, deep green discoloration of the clinical crowns, enamel hypoplasia and areas of enamel decalcification (white spot lesions), gingival bleeding, and a subtle soft tissue swelling localized to the buccal aspect of the mandibular right first primary molar. The child received comprehensive oral treatment under general anesthesia. Clinical inspection revealed areas of exposed dentin and undermined enamel, and both

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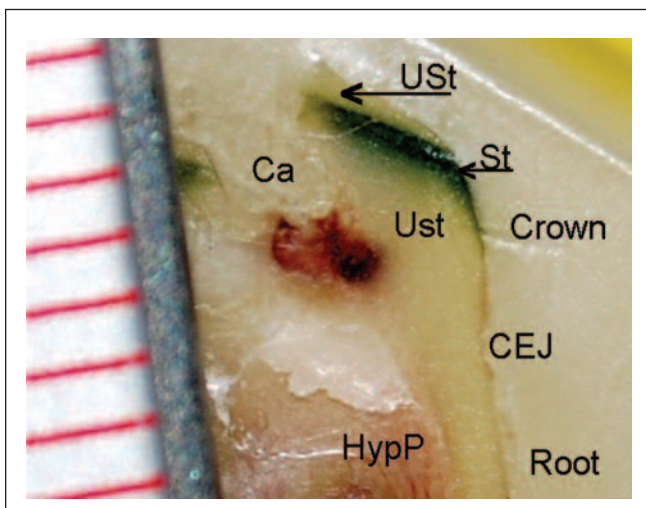
mineralized tissues appeared to be clinically affected by the green discoloration (Figure 1). The infected mandibular right first primary molar and a mandibular left second primary molar with a carious pulp exposure and the pulp showing abnormal color and profuse bleeding were extracted. The primary mandibular left second molar was subjected to histological examination.

Visual examination of the paraffin embedded unstained tooth sections revealed the following in an occlusal-gingival direction: a narrow band of unstained dentin; a stained band of dentin parallel to the external morphology of the tooth becoming thinner in a gingival direction until it “disappeared” in the gingival third of the crown; unstained dentin between the stained band of dentin and the pulp (Figure 2). Microscopic examination of sections of the extracted tooth stained with hematoxylin and eosin did not show green stained dentin but a narrow band of more obscure dentin parallel to the morphology of the tooth, hyperemic pulp tissue,

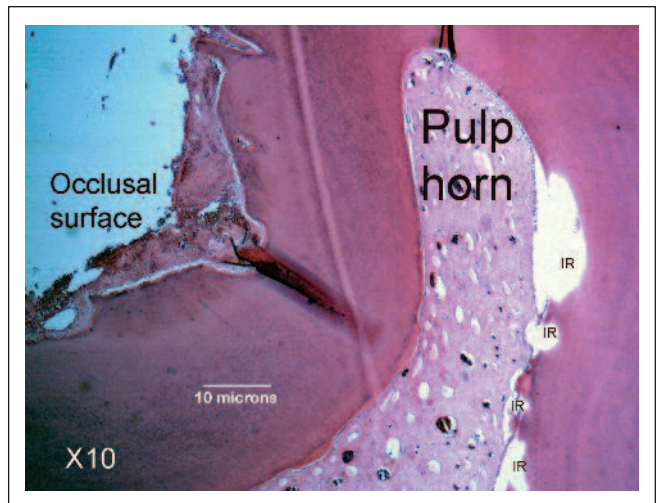
internal resorption, irregular dentin tubules, and an irregular cemento-dentin junction (Figures 3-5).



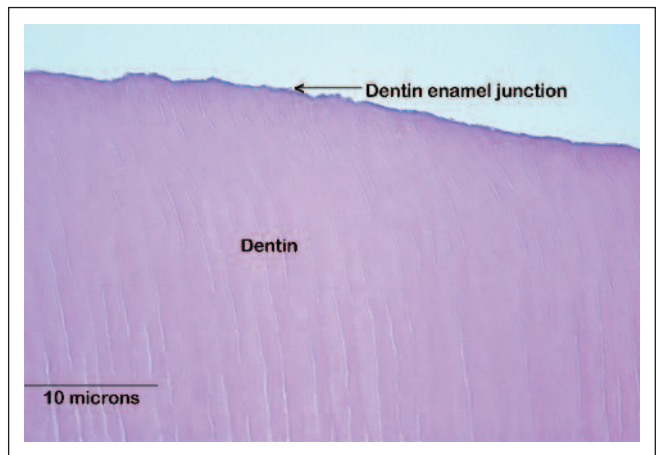
**Figure 1.** Clinical picture of primary maxillary left mandibular molars showing hyperbilirubinemia stain affecting enamel and dentin, caries and enamel hypoplasia.



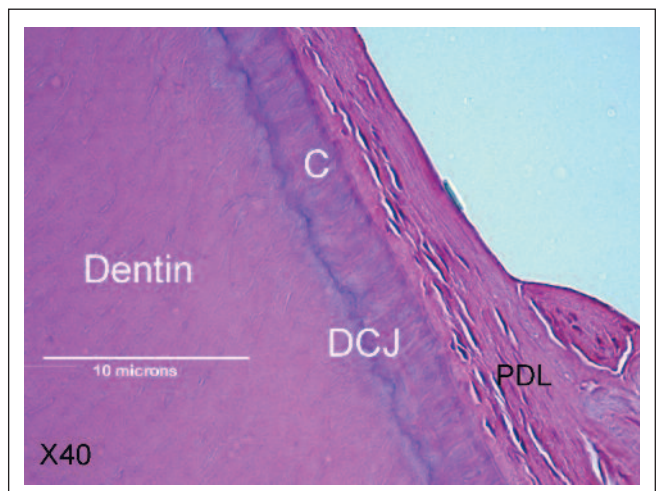
**Figure 2.** Histological block picture showing areas of caries (Ca), unstained dentin (Ust), stained dentin (St), and hyperemic pulp (HypP). CEJ= cemento-enamel junction. The ruler on the left side is on mm.



**Figure 3.** Microscopic image showing an inflamed pulp, areas of internal resorption (IR) and a band of dentin with accentuated stain parallel to the occlusal surface (stained with hematoxylin and eosin).



**Figure 4.** Microscopic image of the coronal dentin area in which irregular dentin tubules are evident (stained with hematoxylin and eosin).



**Figure 5.** Microscopic image of the root surface showing irregular dentin tubules and an irregular dentin-cementum junction (DCJ) (stained with hematoxylin and eosin, PDL= periodontal ligament).



## DISCUSSION

The presence of enamel hypoplasia in the present case is consistent with previous reports that indicate that 50% of children with CF may develop enamel hypoplasia,<sup>8</sup> and a comparison of individuals with CF and healthy control individuals that indicated that demarcated enamel opacities in the primary dentition were present in 16% and 7% cases respectively, demarcated enamel opacities in the permanent dentition in 39% and 11% cases respectively, and diffuse opacities in 17% and 15% cases respectively.<sup>12</sup>

Green intrinsic HypB discoloration of the teeth is extremely uncommon and appears mostly in the primary dentition, without a gender susceptibility; Belanger *et al*<sup>13</sup> described the oral and systemic findings of 11 children with biliary atresia, 4 of them with green staining of the primary teeth and the gingival tissues; Guimarães *et al*<sup>8</sup> reviewed 47 cases in the literature and reported one more case; Naudi *et al*<sup>10</sup> reviewed 52 published cases and contributed 2 new reports to the literature. Intrinsic staining of the primary teeth in CF patients was previously related to the use of Tetracycline before pediatricians were aware of the staining effect on developing teeth by Tetracyclines.<sup>14</sup> The oral manifestations in children with liver failure may include HypB related green staining of the teeth and gingiva (61.3% of children).<sup>7,8,10</sup> Guimarães *et al*<sup>8</sup> found that HypB related discoloration may be caused by biliary atresia in 58.1% of the children, by hemolytic disease in 30.2%, biliary hypoplasia in 2.3%, and by cholestasis in 2.3% of the children, and Lin *et al*.<sup>7</sup> identified a similar proportion of patients (61.3%) with biliary atresia and a HypB discoloration of the dentition. While calcified dental tissues may develop a permanent green discoloration, the oral soft tissues (pulp, gingiva, and periodontal ligament) may develop a temporary stain due to their continuous metabolism.<sup>7,11,15</sup> Accordingly, since the HypB took place in the present case before age 9 months and he appeared in our clinic at age 3-year, no soft tissue clinical or histological HypB related stain was evident.

It appears that there is some disagreement as to the localization of the intrinsic discoloration in the literature; enamel and dentin, prenatally formed enamel caps, or predominantly affecting the dentin with the stain scattered through enamel.<sup>7,9</sup> In addition it has been noted that in mice the pre-enamel and pre-dentinal tissues may be affected with experimental bile obstruction,<sup>11</sup> and previous and the present report describe the discoloration limited to the crown (Figure 2) while others describe a deeply stained root discovered upon extraction prior to liver transplantation.<sup>11</sup>

The child in the present case was diagnosed with CF soon after birth, followed by hyperbilirubinemia and liver transplantation at 10 months of age. Therefore, it is not unexpected that the oral tissues were affected by such significant disease and their respective treatments during this critical period of dental development. The abnormal clinical appearance of the crowns of the primary dentition (Figure 1), including enamel staining and hypoplasia and the HypB discolored coronal dentin evident via inspection through open carious lesions and the histological block (Figures 1 and 2)

confirmed the hepatic disease as the source of the intrinsic stain. The microscopic examination of the hematoxylin-eosin (H&E) stained specimens did not show any green stain but yet, a more stained band parallel to the tooth morphology (Figure 3), similar to the one seen in the block examination, is evident; this apparently being the outcome from the process of histological staining with H&E.

The findings from the present histological examination of an HypB stained tooth are in agreement with a previous report that indicates that HypB may be related to irregular dentin (Figure 5) that develops prior to liver transplantation.<sup>16</sup> Interesting is the finding of an irregular cemento-dentin junction and irregular dentin tubules in the root (Figure 4); the fact that this area developed after the liver transplantation suggest that these anomalies were related to the liver transplantation and its subsequent systemic effects and/or treatment.

## CONCLUSIONS

The present and previous manuscripts indicate that hyperbilirubinemic staining of primary teeth affects dental hard tissues at the time of their calcification, and the clinical picture of the stain may be related to stained enamel and/or dentin, and underlying stained dentin visible through translucent unstained enamel.

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